

Heller Ehrman LLP
Attorney Docket No. 40923-0067 US5

U.S. Serial No. 10/713,268
GOVINDAN

REMARKS

Claims 11-20 and 23-32 are pending. Claims 23, 25 and 28 have been amended. Claims 14-15 and 26-27 have been withdrawn from consideration. In the office action issued March 8, 2005, claims 11-13, 16-20, 23-25 and 28-32 were rejected under 35 USC § 112, second paragraph, as indefinite. Claims 11-13, 16-18, 23-25 and 28-30 were rejected under 35 USC § 103(a) as obvious over Strobel and Govindan (Bioconjugate Chemistry, hereafter "Govindan I"). Claims 11-13, 16-20, 23-25, and 28-32 were rejected under 35 USC § 103(a) as obvious over Strobel and Govindan in view of WO99/11294 (Govindan II). The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 11-13, 16-20, 23-25 and 28-32 are rejected under 35 USC § 112, second paragraph, as indefinite. Specifically, the Examiner alleges that 11 and 23 are indefinite for failing to specify the location of the recited linker group. Claims 23 and 25 are rejected for alleged lack of antecedent basis. Applicants respectfully traverse.

Section 112, second paragraph, requires only that the claims, read in light of the specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention, in language as precise as the subject matter permits. *Shatterproof Glass Corp. v. Libbey-Owens Ford Co.*, 758 F.2d 613, 225 USPQ 634 (Fed.Cir.1985). In the instant case, the Examiner fails to offer any reasoning as to why it is necessary to specify the location of the linker group, nor why one skilled in the art could not recognize the point of attachment of the linker to a composition within the scope of the instant claims. In the absence of any explanation the rejection is improper and should be withdrawn.

The instant claims recite methods using a composition that contains a peptide containing two defined amino acids (D-tyrosine and a basic D-amino acid) where the basic D-amino acid is at the C-terminus of the peptide. The claim specifies that there are no contiguous L-amino acids between the D-tyrosine and the carboxy terminus. The peptide also contains a linker for covalently joining the peptide to the antibody. The linker could be attached to any suitable attachment point in the peptide including, for example, at the N-terminus or at a point between the two defined amino acids. As such, the linker would be instantly recognizable to one skilled

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in the art. This is all that is required for compliance with § 112, second paragraph. To force applicants to specify a particular location of the linker would unfairly limit the scope of applicant's claims and invite appropriation of the invention by one who would merely place a linker in a different location than that specified. Applicant respectfully submits that one skilled in the art is readily apprised of the utilization and scope of the claimed invention and that the claims fully comply with § 112, second paragraph. Accordingly, withdrawal of the rejection respectfully is requested.

Claims 23 and 25 are rejected for alleged lack of antecedent basis. Applicant has amended claims 23 and 25, thereby mooting the rejection.

Rejections under 35 U.S.C § 103(a)

Claims 11-13, 16-18, 23-25 and 28-30 are rejected under 35 USC § 103(a) as obvious over Strobel and Govindan (Bioconjugate Chemistry, hereafter "Govindan I"). Claims 11-13, 16-20, 23-25, and 28-32 are rejected under 35 USC § 103(a) as obvious over Strobel and Govindan in view of WO99/11294 (Govindan II). Applicants respectfully traverse.

When combining references to make out a *prima facie* case of obviousness, the examiner is obliged to show by citation to specific evidence in the cited references that (i) there was a suggestion/motivation to make the combination and (ii) there was a reasonable expectation that the combination would succeed. Both the suggestion/motivation and reasonable expectation must be found within the prior art, and not be gleaned from applicants' disclosure. *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988); *W.L. Gore v. Garlock, Inc.*, 220 USPQ 303, 312-13 (Fed. Cir. 1983) (holding that is improper in combining references to hold against the inventor what is taught in the inventor's application); *see also* MPEP §§ 2142-43 (August 2001). In the present case, the Examiner has failed to set forth adequate reasons as to why one of ordinary skill in the art would have been motivated to combine the cited references to arrive at the instantly claimed invention and therefore no *prima facie* case of obviousness exists, and the rejection should be withdrawn.

The Examiner states that Strobel teaches the use of a sugar-linked tyramine to radioiodinate proteins. Strobel does not, however, teach use of peptides containing D-Tyr or D-Lys. The Examiner then seeks to argue that one skilled in the art would have been motivated to

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modify the methods described by Strobel because of the deficiencies of the Strobel methods as described by Govindan I. Govindan I is cited as teaching a peptide comprising a D-Tyr and D-Lys that can be used for radioiodination. The Examiner's arguments fail on at least two grounds.

First, even if Govindan provided a motivation to modify the methods of Strobel, there would have existed no motivation for one of ordinary skill in the art to modify Strobel to arrive at the instantly claimed invention. Rather, Govindan would have motivated the skilled routineer to use the Govindan methods, which do not employ a carbohydrate residue. Why would one of ordinary skill in the art, provided with the improved methods described by Govindan, been motivated to somehow combine Strobel and Govindan, rather than utilize the ready-made improvement provided by Govindan? There simply is no suggestion in either reference to combine the references to arrive at applicant's instantly claimed methods. Applicants respectfully submit that the Examiner is relying on improper hindsight to find a motivation that is not present in the references. No *prima facie* case of obviousness exists and withdrawal of the rejection respectfully is requested.

Second, nothing in the combination of Govindan and Strobel would have led the skilled artisan to applicant's instantly claimed methods. The Examiner quotes Strobel as stating that the likely site of attachment of the Strobel conjugate is via the epsilon amino group of lysine residues. The relevance of this statement is not understood. This statement in Strobel clearly refers to the side chains of lysine residues on the protein to be conjugated and not to any lysine in the Strobel conjugate. Applicant's methods use peptides containing a D-lysine that is used to covalently link a reducing sugar via the lysine side chain. The peptide is then conjugated to a protein via a distinct linker moiety. This conjugation approach is quite different from that described by Strobel.

Moreover, Strobel fails to teach or suggest the use of a tyrosine containing *peptide* for conjugation to protein. Govindan I teaches the use of a tyrosine containing peptide for conjugation to protein but fails to teach or suggest that the peptide should be conjugated to a carbohydrate residue, let alone that the carbohydrate should be conjugated to the lysine side chain. Indeed, in Govindan I the lysine side chains are used for coupling of metal chelating residues, rather than coupling to carbohydrate. Nothing in either reference, either alone or in combination would have motivated one of ordinary skill in the art to use methods that employ a

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peptide having the very specific structure recited in the instant claims. Accordingly, no *prima facie* case of obviousness exists and withdrawal of the rejection respectfully is requested.

Govindan II is cited merely for the proposition that melibiose could be substituted for the dilactitol described by Strobel. However, Govindan II fails to remedy the deficiencies of the combination of Strobel and Govindan II described above, and therefore the rejection of claims 11-13, 16-20, 23-25 and 28-32 also should be withdrawn.

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CONCLUSION

In view of the above remarks and amendments, it is respectfully submitted that this application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to telephone the undersigned at the number listed below if the Examiner believes such would be helpful in advancing the application to issue.

If any additional fees are required for the filing of this paper, applicants authorize the Commissioner to charge any deficiency to Deposit Account No. 08-1641.

Respectfully submitted,



Date: August 8, 2005

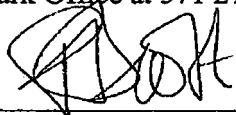
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